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THE EYE BANK AND CORNEAL GRAFTING PROGRAM*

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IT HAS BEEN ESTIMATED that there are approximately 1500 persons in Canada whose vision could be benefited by corneal transplantation. Many of these are in the blind category and do not possess funds for travel to corneal transplanting centres in foreign countries. Others who could meet the expense are unwilling to go far afield for the long period of hospitalization and postoperative care required for keratoplasty.

In Canada, few surgeons have had training in the technique of keratoplasty, or have been willing to undertake several years of research and special study in this field. Nevertheless, a number of corneal grafts on favourable cases have been performed in this country. Progress in this field has been hampered by the difficulty of obtaining suitable eyes.

It was apparent that if the benefits of corneal grafting were to be made available to Canadians, financial aid would be necessary from government or private agencies to assist patients in travel, hospitalization, surgery and postoperative convalescence (such aid has been given frequently in the past by the Canadian National Institute for the Blind). Alternatively a program of training could be undertaken in teaching centres where patients could be brought to properly equipped institutions and operated upon by surgeons skilled in the special techniques and acquainted with the fundamental problems in this field.

In order to promote a program of corneal grafting, it was first necessary to set up an eye bank for receiving and distributing donor eyes. It was felt that initially the donor material would come largely from enucleated eyes (intraocular tumours, absolute glaucoma, etc.) where the cornea was not affected by the disease processes, and that eventually persons in the older age groups would donate their eyes so that after death they could be used for corneal grafting. Since the dead body becomes the property of the next-of-kin, the act of willing one's eyes is not sufficient but does place an obligation upon the relative, who in most instances gives permission for the removal of the eyes after death.

Since 1945, in the United States, a number of eye banks have been organized. In order to obtain sufficient donor material, it has been found necessary to publicize the need for eyes and to acquaint the public with the benefits of corneal grafting. This program has been handled almost exclusively by eye bank staffs under medical supervision. However, in Canada, the Canadian Ophthalmological Society has authorized the Canadian National Institute for the Blind to undertake the organization of an "Eye Bank Service" which will include publicity to lay groups and to the press, the registration of donors, and the distribution of eyes. Since this organization is Canada-wide, the publicity can be national in extent, and the distribution of eyes can be facilitated by their branches throughout the country.

THE EYE BANK LABORATORY

In its simplest form, an eye bank laboratory may consist of a refrigerator for storage at 4° C. and a thermos flask which can be packed with wet ice for shipment of eyes. For any large-scale corneal grafting program, however, such a simple eye bank is inadequate. University centres with training programs in ophthalmology are best suited to operate an eye bank, since it requires the services of ophthalmic residents to enucleate eyes, an ophthalmologist to examine the eye

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for suitability for grafting, and some special technical knowledge in the storing and shipping of the eyes.

THE UNIVERSITY OF TORONTO EYE BANK LABORATORY AND RESEARCH PROGRAM

In 1955, a National Health Grant was obtained by the University of Toronto for the organization of an eye bank and to support a program of research on the problems of corneal grafting. The time was propitious for such an endeavour, since antibiotics and steroids were improving the chance of success of corneal grafting and newer techniques and instruments were simplifying procedures.

The immediate problem to be dealt with in the laboratory was that of the storage of donor eyes. It had been shown by many workers in the past that success in corneal grafting depended upon viable clear cornea for donor material. This corneal clarity is influenced by such factors as the nature of the death of the donor, the time of enucleation after death, the duration, medium, and temperature of storage. Eyes may be removed up to 10 hours after death if the body has been refrigerated, and it is possible to store enucleated eyes in the ordinary refrigerator at 4° C. up to four days. Liquid paraffin has been found to be a better medium for storage than aqueous vapour or normal saline. Eyes pre-treated in 15% glycerin for one hour and deep-frozen at −79° C. are seldom used because of the lack of experience with such tissues up to the present time, but it is known that lamellar grafts can be taken from eyes stored in this way and used successfully, whereas full-thickness grafts have not received adequate trial.

Since it is generally agreed by keratoplasty surgeons that the cells in the graft must be viable at the time of grafting, a study was made of the viability of corneal epithelial cells and fibroblasts both in tissue culture[1] and on the chorioallantoic membrane of the embryonated hen's egg.[2] It was found that rabbits' corneæ stored at 4° C. remained viable up to three weeks in liquid paraffin, and up to two weeks in aqueous vapour. In eyes pre-treated in glycerin and quick-frozen, viability of the cells did not persist beyond a few hours of storage, but when the jars containing the eyes were wrapped in gauze to slow the freezing process, the cells remained viable for at least three months.

It was noted during these experiments that in eyes stored at 4° C. the corneæ became cloudy long before the cells became non-viable, whereas those which had been quick-frozen and stored at −79° C. remained clear throughout the period of storage even though they were non-viable. A study of water-soluble corneal proteins was therefore undertaken, and it was shown by electrophoresis that at the end of the first week of storage at 4° C. the four globulin fractions began to coalesce into one, whereas in deep-frozen eyes no change in the protein fractions occurred throughout storage.[3] It seems possible, therefore, that the clouding in donor corneæ during storage is due to changes in proteins rather than to loss of viability.

It has long been known that skin homografts are seldom successful. In the avascular cornea, however, a homoplasty is possible, since a graft will heal and remain clear in a high percentage of cases. The late clouding of corneal grafts, occurring from three weeks to two years after grafting in humans, is unpredictable, and is thought to be due to a donor-recipient sensitivity reaction. Experiments were undertaken in the study of this important problem using the interlamellar method of grafting in rabbits. It was found in a series of grafts that 30% developed reactions, and that these only developed when blood vessels invaded the graft bed postoperatively, and therefore depended upon the presence of humoral antibody. When skin (which has the same antigenic properties as cornea) from the same animal was simultaneously grafted into the belly of the recipient, the corneal graft opacities increased from 30 to 80%, but if skin from another animal was grafted into the belly, the reactions increased to only 35%.[4] Thus, the donor-recipient reaction is a highly specific one, and the increase in corneal graft reactions when skin grafting is carried out simultaneously is due to the increase in the dose of antigen in the recipient animal.

CLINICAL PROGRAM

It is hoped that, within the next few years, teams will be set up in university centres across Canada to whom cases for diagnosis and subsequent keratoplasty can be directed. At the Toronto General Hospital, both the clinical and laboratory aspects of the corneal grafting program are under the direction of one individual. In this way, all aspects of the work are co-ordin-

ated, and it has been possible to correlate laboratory findings with clinical problems, and to acquire techniques by animal experiment. It has been possible to carry out a training program for ophthalmologists both in the laboratory and in the operating room by including a visiting ophthalmologist in the research team, and a junior staff member in the surgical team.

Since the institution of this program, 35 keratoplasties have been performed by this team. All have been surgically successful and some improvement in vision has resulted in most cases. Graft opacification due to a typical antigen-antibody reaction occurred in one patient with conical corneæ six weeks postoperatively, and two other patients with interstitial keratitis developed delayed graft opacification. Eight eyes with conical corneæ had successful full-thickness grafts, resulting in vision ranging from 20/20 to 20/40. In ten patients with severe recurrent metaherpetic keratitis, ten-millimetre lamellar grafts were performed, resulting in visual improvement in all cases and complete remission of symptoms, and there have been no recurrences of the herpetic infection. In the over-all group of 35 cases, a longer follow-up will be necessary to establish the virtue of grafting in various diseases, but at this time it is felt that the scope of keratoplasty may be enlarged to include corneal scars due to chemical burns, a major cause of corneal blindness in Canada.

FUTURE PROGRAM

During the past year, 35 eyes suitable for keratoplasty have passed through the University of Toronto Eye Bank Laboratory. The majority of these eyes came from enucleations performed in Toronto hospitals. It would appear at this time that the quantity of donor material needs to be doubled, and this can be accomplished only if individuals donate their eyes after death. In order to accomplish this, a program of publicity will be undertaken to acquaint the public with the need for such material. Fortunately the corneæ of older persons are ideal for grafting, and in time they should be the main source of donor material.

Methods of storage of eyes which are not immediately required for transplanting must be improved, if wastage of good donor material is not to occur. It seems likely that methods of deep freezing will be worked out soon, but extensive clinical trial with frozen material will depend upon prior experimentation in the laboratory.

The unpredictability of corneal clouding will remain a problem for some years to come, but when we fully understand the causes for this clouding, it will be possible to prevent or suppress the reaction with suitable therapy. Reoperation in such cases has frequently resulted in clear grafts, and one failure should not prejudice further trial in individual cases. Future research may develop some means of anticipating reactions between donor and recipient.

The use of animal or avian tissues for corneal grafting in humans should now be reinvestigated because of the universal availability of such tissues. This is particularly necessary for a country such as India where potentials for corneal grafting are very great, and where there are many difficulties in obtaining eyes from dead bodies. In preliminary experiments on rabbits, we have shown[5] that 70% of interlamellar chicken grafts remain clear, whereas 60% of duck and 50% of turkey grafts remain clear. Avian tissues were all superior to beef, lamb, and monkey corneæ. In the event that supplies of good human donor eyes become inadequate, it seems certain that clinical trial with avian or animal tissues will be carried out.

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FULMINATING POSTOPERATIVE STAPHYLOCOCCAL BRONCHOPNEUMONIA

Fulminating postoperative staphylococcal bronchopneumonia following pulmonary valvulotomy in an 11-year-old girl operated on under hypothermia was not diagnosed till autopsy; serial radiographs showed a spreading lesion of the lung. Cultures taken from the anæsthetist, the throat of the patient 10 days preoperatively, and the instruments used were negative. It is postulated that the patient became a throat-carrier of staphylococci after the preoperative throat culture and that bilateral thoracotomy and hypothermia diminished resistance so that the organism gained a strong hold. The only line of treatment suggested is massive therapy with a broad-spectrum antibiotic, such as erythromycin or chloramphenicol.—G. M. Wyant and E. M. Nanson, *Ann. Surg.*, 145: 133, 1957.